CXXXIV. THE CONSTITUENTS OF *FABIANA IMBRICATA*.

By GLYN REES EDWARDS and HAROLD ROGERSON.

From the Chemical Department, Liverpool University.

(*Received June 20th, 1927.*)

The plant *Fabiana imbricata* (Ruiz and Pavon) or *pichi-pichi* is a well-known shrub growing in South America and belongs to the Solanaceae.

It has been used medicinally for centuries by the Incas, and about 50 years ago attracted some attention in Europe as a specific for urinary and liver complaints.

The first chemical examination appears to have been carried out by Nivière and Lotard [1887], who state definitely that the drug is free from alkaloid. They ascertained the presence of a fluorescent principle, a yellow precipitate with lead acetate analogous to "l'esculo-tannate de plomb," gummy matter, glucose and calcium tartrate.

A more detailed examination was carried out, however, by Kunz-Krause [1899], who found the leaves to contain choline, chrysotropic acid (now known as scopoletin) and a substance which he called "fabioglucotannoid" and for which he suggested the formula:

$$C_6H_{11}O_5.O.C_6H_2(OH)(OMe)CH : CH.CO_2H$$

or its internal anhydride. The compound was described as a yellow, very hygroscopic substance softening at 80° and beginning to swell up at 105°.

Kunz-Krause further isolated from the wood a volatile oil which he called fabianol (no formula given) together with a non-volatile white crystalline solid melting at about 280° and capable of being sublimed. This was called fabianaresen and the formula was $C_{54}H_{90}O_6$ although cryoscopic determinations indicated $C_{18}H_{30}O_2$.

It is evident that Kunz-Krause isolated products of doubtful purity, and the results obtained in the present investigation have confirmed this, more especially in regard to the so-called fabioglucotannoid.

This substance has now been shown to be a new glucoside of scopoletin for which the name *fabiatrin* is proposed, and its properties are described in the experimental part of this paper.

The authors have been unable to confirm the presence of choline, but have indicated the presence of a basic substance which forms a picrate. In addition, a saponin has been detected, and the physiological effect of the plant appears to be due entirely to this substance. Although the drug is classified among the Solanaceae, the absence of alkaloids is confirmed.

Experimental.

The material used in this investigation consisted of twigs about 3 feet in length and varying in diameter from 1 to 2 inches. The cortex was very thin, and the wood extremely hard. The drug possessed a characteristic odour, and a substance (alcoholic) was isolated possessing the odour in a marked degree.

The twigs were very kindly ground for us by Messrs Evans, Lescher and Webb, Ltd., and we would here express our deep appreciation to C. J. S. Sendall, Esq., for the help so readily given.

As a preliminary experiment, 50 g. of the ground material were successively extracted in a Soxhlet apparatus, when the following amounts of extract, dried at 100°, were obtained.

Light petroleum (B.P. 29–45°) extracted		0·44 %
Ether	,,	0·56 ,,
Chloroform	,,	1·40 ,,
Ethyl acetate	,,	1·07 ,,
Alcohol	,,	1·52 ,,
	Total	4·99 %

In order to glean some idea of the nature of the drug, two portions (500 g. each) were treated respectively with (*a*) sodium carbonate (30 g.) and (*b*) hydrochloric acid (2 %).

(*a*) On distillation in steam, 0·7 g. of an essential oil was obtained which was neutral, and contained no furfuraldehyde. The aqueous distillate was also neutral, thus proving the absence of volatile bases.

(*b*) In this case the acidic solution was filtered from the marc, and although the filtrate gave the usual alkaloidal reactions, only resinous products were obtained.

For the purpose of a complete examination of the drug, a quantity (5 kg.) of the ground material was thoroughly extracted with light petroleum, ether and alcohol.

Examination of the light petroleum extract.

After the removal of the solvent, there remained a dark green viscous mass amounting to 15 g. The residue was taken up in ether when, on keeping, a small quantity of sparingly soluble substance separated as a white amorphous powder. This was collected and washed thoroughly with ether when it was found to melt between 74° and 77°; and, after recrystallisation from ethyl acetate, it was obtained in colourless plates melting at 82° (found, C = 78·05 % and H = 12·7 %). On hydrolysis with alcoholic potash, an alcohol melting at 80° and an acid melting at 77·5–78° were obtained. The above compound is evidently an ester, and in view of the subsequent isolation of arachidic acid, it is very probable that the acidic portion of the ester is also arachidic acid.

The ethereal liquid, after the removal of the above-described ester, was extracted with solutions of ammonium and sodium carbonates, and 5 % sodium hydroxide.

The ammonium carbonate removed a mere trace of substance.

The sodium carbonate removed 0·1 g. of an acid which, when recrystallised from ethyl acetate, melted at 62°. This acid was probably palmitic acid, but the amount obtained was too small to confirm by analysis.

The sodium hydroxide also removed a further small quantity of the acid melting at 62°.

The ethereal liquid, containing the neutral portion of the extract soluble in light petroleum was finally dried over anhydrous sodium sulphate and the solvent removed, when there was left a quantity of viscous product. This was hydrolysed with alcoholic potassium hydroxide, and worked up in the usual manner for the isolation of the unsaponifiable constituents and the combined fatty acids. In this way there were isolated (*a*) a phytosterol (M.P. 134°) which gave an acetyl derivative melting at 117°; (*b*) a *new* unsaturated alcohol (B.P. 145°/25 mm.) agreeing with the formula $C_{26}H_{42}O$ (found: C = 84·6 %; H = 11·3 %. Calc. for $C_{26}H_{42}O$: C = 84·8 %; H = 11·3 %). This alcohol possesses the characteristic odour of the drug and appears to be the odoriferous principle; it gave the colour reactions of the phytosterols; (*c*) traces of unsaturated fatty acid and (*d*) arachidic acid (M.P. 77°). (Found: C = 76·6 %; H = 13·0 %. Calc. for $C_{20}H_{40}O_2$: C = 76·9; H = 13·0 %.)

Examination of the ethereal extract.

This was a dark green soft solid amounting to 20 g. It gave only (*a*) a grey amorphous solid (M.P. 86°) and (*b*) a colourless crystalline substance (M.P. 82°), both being insufficient to identify. There was a complete absence of any glucoside in this extract.

Examination of the alcoholic extract.

This extract consisted of a dark coloured resin amounting to 150 g. It was mixed with water, and the mixture distilled in a current of steam. The distillate contained a small amount of volatile oil, but nothing acidic or basic. After the above operation, there remained in the flask an orange-coloured aqueous liquid together with a quantity of dark brown resin. The latter amounted to 40 g., from which nothing definite was isolated.

Examination of the aqueous liquid.

This liquid, after being separated from the resin, was concentrated *in vacuo* to about one litre and repeatedly extracted with ether.

Isolation of scopoletin, $C_{10}H_8O_4$. The ethereal extracts were united and concentrated to small volume, when, on keeping, 7 g. of a pale yellow solid separated. This was collected and recrystallised from alcohol, giving pale yellow needles (M.P. 204°), and a brilliant blue fluorescence with alkalis. The

substance was identified with scopoletin. (Found: C = 62·5 %; H = 4·18 %. Calc. for $C_{10}H_8O_4$: C = 62·5 %; H = 4·2 %.)

An *acetyl* derivative was prepared which separated from alcohol in slender colourless needles, M.P. 177°. (Found: C = 61·25 %; H = 4·4 %. Calc. for $C_{10}H_7O_4.COCH_3$: C = 61·5 %; H = 4·3 %.)

After washing the ethereal solution and drying, 0·1 g. of a pale yellow solid separated on keeping for a short time. It was found to be phenolic in character, but it was quite amorphous and had no definite melting point.

Isolation of a basic principle. The original aqueous liquid, after being extracted with ether as described above, gave precipitates with the usual alkaloidal reagents and possessed a bitter taste. A portion of the solution was therefore made alkaline with sodium carbonate and repeatedly extracted with ether. The ethereal extracts were united, dried and the solvent removed, when there remained a small quantity of a gummy mass. The product contained nitrogen and gave reactions for an alkaloid. It could not be obtained crystalline. A solution in hydrochloric acid gave a brown amorphous product with mercuric chloride, and a *picrate* was readily formed which was soluble in hot alcohol, but separated in the amorphous state, melting with decomposition at 125°. No crystalline derivatives could be prepared.

The remainder of the aqueous liquid was concentrated *in vacuo* to a syrup, and a small portion of the latter was treated with phenylhydrazine acetate, when an osazone separated. This was recrystallised from dilute pyridine, when it melted at 210° thus being identified as *d*-phenylglucosazone.

Isolation of a hitherto undescribed glucoside of scopoletin. The concentrated aqueous liquid was mixed with a quantity of absolute alcohol when a precipitate separated. This redissolved on warming and again separated on cooling as a brown solid.

After filtration the substance was recrystallised from dilute alcohol using a little charcoal to remove colouring matter, when it separated in rosettes of needles melting at 226–228°.

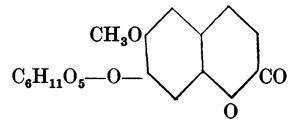
The compound gave scopoletin and glucose on hydrolysis with dilute acid, and analysis proved it to be the glucoside of scopoletin having the formula $C_{16}H_{18}O_9$, $2H_2O$. Dried at 100°. Found: C = 48·7 %; H = 5·6 %. Calc. for $C_{16}H_{22}O_{11}$: C = 49·2 %; H = 5·6 %. Dried at 130°. Found: C = 51·2 %; H = 5·35 %. Dried at 160°. Found: C = 51·27 %; H = 5·3 %. Calc. for $C_{16}H_{20}O_{10}$: C = 51·6 %; H = 5·3 %.

It was found impossible to remove the second molecule of water, and a separate determination of the substance dried at 160° showed a loss of 4·6, the calculated amount for $1H_2O$ being 4·8 %.

The above glucoside has not been described hitherto in the literature and it is proposed to designate it *fabiatrin*.

Fabiatrin is a colourless solid which crystallises in needles, readily soluble in hot water, but very sparingly soluble in the usual organic solvents in the cold. The aqueous solution gives a yellow colour with ammonia and caustic

soda, indicating the opening of the pyrone ring, and the constitution of the glucoside may be represented thus:



Isolation of a saponaceous substance. The dilute alcoholic solution of the syrup, after the removal of the glucoside, was concentrated to small volume and kept for some days. A further quantity of fabiatrin separated, the total amount obtained being 7 g. After removal on the filter, the filtrate was digested with a quantity of absolute alcohol, when a brown amorphous solid separated, whose properties indicated that it belonged to the saponins. A very dilute aqueous solution produced a foam which remained stable for many days. It possessed an exceeding bitter taste, but in the dry state was not sternutatory.

Physiological tests.

These test were kindly conducted by Prof. W. J. Dilling and the results (indicated briefly) show that the drug is poisonous to animals, a decoction having proved fatal to frogs, rabbits and cats. The poisoning effect appears to be due to a saponin, and such a substance has been shown to be present.

A separate examination of scopoletin has shown this substance to be quite inert, both physiologically and bacteriologically—the latter experiments being kindly done by Prof. J. M. Beattie.

The physiological action of fabiatrin will be described in due course.

Summary.

A complete examination of the aerial stems of *Fabiana imbricata* (Ruiz and Pavon) has been conducted, and the following substances have been isolated. A neutral essential oil which gave a negative reaction for furfuraldehyde; an ester (M.P. 77·5–78°); palmitic acid; a phytosterol (M.P. 134°); a new unsaturated *alcohol*, $C_{26}H_{42}O$ (B.P. 145°/25 mm.), possessing the fragrant odour of the drug; traces of unsaturated acids; arachidic acid; scopoletin; a basic compound which gave an amorphous picrate (M.P. 125° with decomposition); a sugar giving *d*-phenylglucosazone; a new glucoside of scopoletin, $C_{16}H_{18}O_9.2H_2O$ (M.P. 226–228°), designated *fabiatrin*; and an amorphous substance possessing the properties of a saponin.

In conclusion, the authors express their warmest thanks to Prof. I. M. Heilbron for suggesting the research; to Dr C. J. MacAlister, F.R.C.P., for his instrumentality in providing the material, and also a grant towards the expenses of the investigation; and to Profs. Dilling and Beattie for conducting the physiological and bacteriological tests.

REFERENCES.

Kunz-Krause (1899). *Arch. Pharm.* **237**, 1.
Nivière and Lotard (1887). *J. Pharm. Chem.* (5), **16**, 389.